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# Influence of Sweeteners on Gut Microbiota

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**Abstract:**

The impact of sweetener intake on the gut microbiota is a topic of increasing interest, given the rising global consumption of both naturally occurring and artificially produced sweeteners as alternatives to traditional sugars. This review seeks to explain how various sweeteners, both natural and artificial, affect the composition and function of gut microbiota. Sweeteners are categorized into natural sources, such as stevia and honey, and those synthesized artificially, including aspartame and sucralose. Natural sweeteners, known for their potential health benefits and minimal side effects, have the potential to stimulate the growth of beneficial bacteria and increase the production of short-chain fatty acids (SCFAs). Conversely, artificial sweeteners have been associated with dysbiosis, potentially resulting in a higher prevalence of harmful bacteria. The research highlights the inconsistency in the effects of artificial sweeteners, which may be influenced by factors such as type, dosage, and individual variability. Despite the existing evidence, the long-term consequences of sweetener consumption on gut health remain unclear, underscoring the need for more comprehensive, well-designed clinical trials. Future research should also aim to develop advanced methodologies for assessing gut microbiota health and explore personalized interventions to address the differential responses to sweeteners.

**Keywords:** Sweeteners, Gut microbiota, Natural sweeteners, Artificial sweeteners, Metabolic health, Dysbiosis

## 1. Introduction

### 1.1 Background: Definition and types of sweeteners

Sweeteners are a group of food addictives which provide sweet taste or enhance the flavor of food. One way for classification is by metabolic influence. There are non-nutritive sweeteners (NNS), and nutritive sweeteners, including sucrose, honey, maple syrup, and high-fructose corn syrup. Another method is based on sources, there are natural sweeteners and artificial sweeteners. Natural sweeteners were extracted from plants or minerals, such as stevioside from *stevia rebaudiana* and erythritol from fermented corn starch. Such sweeteners are usually known for having few toxic side effects. Artificial sweeteners are prepared through chemical synthesis, such as

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saccharin, aspartame, sucralose, etc. Both natural and artificial sweeteners are known for being highly sweet, low in calories, soluble, and stable. Natural sweeteners are usually considered safer, while artificial sweeteners have been suspected of causing cancer. However, both artificial and natural sweeteners intake should be in moderate amounts as part of an overall healthy diet and lifestyle, taking into consideration balanced eating habits and wellness practices.

### 1.2 Importance of research: Prevalence of sweeteners in modern diets

The global use of sweeteners in foods is on the rise, particularly among those looking for healthier sugar alternatives. Although FDA and ESFA consider a variety of sweeteners safe, there is no shortage of sceptics. Some researchers doubt non- and low-calorie sweeteners for their safeness in comparison to regular sweeteners, and how sweeteners influence gut microbiota is highly regarded. Hence, studying the way different types of sweeteners impact the composition and function of gut microbiota and their prevalence in modern diets is of significant importance.

### 1.3 Objectives and scope of the review

This article studied the potential effect of sweeteners on gut microbiota from nutriology and microbiology perspectives, and aims to helping understanding biological safety and evaluate the influence of sweeteners on public health.

## 2. Classification of Sweeteners

This study classifies sweeteners by sources, natural sweeteners can be extracted directly from plants, artificial sweeteners can be composed in chemical laboratories.

### 2.1 Natural Sweeteners

Many natural sweeteners not only provide sweetness, but may also contain beneficial nutrients such as minerals and vitamins. Compared with artificial sweeteners, natural sweeteners have a more complex metabolic process in the human body and may have different effects on blood sugar and insulin response. Although natural sweeteners are generally considered safer than artificial sweeteners, it is still important to be aware of the trace amounts of harmful elements that individual ingredients may contain. Some studies have also shown that bioactive ingredients such as phenols, carotenoids, and flavonoids in natural sweeteners have antioxidant, anti-inflammatory, antiviral, and antibacterial properties that not only help prevent disease, but also give food products a longer shelf life.

Historically, honey was the predominant sweetener in human diets. By the 18th century, the consumption of sucrose extracted from beets and sugarcane began to increase dramatically. Lately, the overconsumption of sugar has emerged as a significant public health concern. There is considerable evidence connecting high sugar intake to a higher risk of non-communicable diseases, including Type II diabetes, obesity, and cardiovascular diseases.

**Table 1 characteristics of natural sweeteners**

| Sweetener | Source | Calories (per gram) | Sweetness (relative to sucrose) | Solubility (in water) | Stability | Active Components |
|---|---|---|---|---|---|---|
| Sucrose | Extracted from sugar cane | 4 | 100% | Good | Stable | - |
| Honey | Produced by bees from flower nectar | ~3.3 | <100% (requires more quantity) | Good | Stable at moderate temperatures; | enzymes, phenolic compounds, methylglyoxal, royal jelly proteins (MRJPs), and oligosaccharides |
| | | | | | may alter flavor if exposed to heat | |
| Maple Syrup | Derived from maple tree sap | ~60 | >100% | Good | Stable, best for low-temperature use | minerals, polyphenols |
| Stevioside | Extracted from the Stevia plant | Virtually 0 | ~200x | Good | Highly stable, even at high temperatures | - |
| Erythritol | Produced from certain bacteria or glucose | 0.2 | ~70% | Good | Highly stable, suitable for cooking/baking | - |

### 2.2 Artificial Sweeteners

**Table 2 characteristics of Artificial sweeteners**

| Sweetener | Calories (per gram) | Bitter Aftertaste | Sweetness (relative to sucrose) | Solubility (in water) | Stability |
|---|---|---|---|---|---|
| Aspartame | Virtually 0 | May impart slight bitterness | ~200x | High | Stable under most conditions |
| Sucralose | Virtually 0 | No noticeable bitterness | ~600x | High | Very stable during processing/storage |
| Saccharin | Virtually 0 | Distinctive bitterness | ~500x | High | Very stable during processing/storage |
| Ace-K (Acesulfame Potassium) | Virtually 0 | No noticeable bitterness | ~150x | High | Very stable during processing/storage |

The development and application of artificial sweeteners involve chemical synthesis, food safety, environmental impact, and consumer health. Artificial sweeteners have been introduced as sugar substitutes since the late 1800s and are intended to provide sweetness without adding calories. These sweeteners are usually sweeter than regular sugar and have low or zero calories, and are therefore favoured by the public for managing weight problems. Future research directions may include the development of artificial sweeteners with higher intensity and better taste, as well as exploring the effects of these sweeteners on specific populations (e.g., pregnant women, children, diabetics). In addition, the development of safe and efficient artificial sweeteners will be a key direction for future development as consumer concerns about the safety of food additives increase.

## 3. Mechanisms of Sweeteners' Impact on Gut Microbiota

### 3.1 Basic functions and importance of gut microbiota

Comprising a highly complex, diverse, and dynamic assembly of microorganisms, the gut microbiota plays a crucial role in sustaining human health. The gut microbiota is in symbiosis with the host and maintains normal physiological processes. Microbes not only interact with the human body but also interact with each other. Intestinal microbiome cross-feeding refers to the process of different bacteria in the human gut through the exchange of metabolites to use each other's metabolites, thereby promoting their respective growth and function[1]. This interaction can be unidirectional or bidirectional and involves multiple types of metabolites[1]. For example, some bacteria can degrade complex carbohydrates such as cellulose and hemicellulose, and these degraded products may become a source of nutrients for other microorganisms[1]. This process might be competitive, influencing abundancy of species.

Numerous studies have found that gut microbiota plays a role in nutrients and metabolism, modulating the immune system, prevent infection, intestinal barrier function and multiple diseases.

### 3.2 How sweeteners affect gut microbiota

#### 3.2.1 Direct effects: Metabolic products of sweeteners on microbiota

Sucrose, honey, and maple syrup, as natural sweeteners that provide energy, are metabolized through the gut and can have a direct impact on the microbiota. Sucrose is a disaccharide containing one molecule glucose and one molecule fructose. It is mostly splitted in the small intestine into two monosaccharides by the enzyme sucrase and absorbed into the bloodstream. Under certain circumstances, such as overconsumption or low sucrase activity in the small intestine, undigested sucrose passes into the gut, where it can be fermented by gut bacteria to produce short-chain fatty acids (SCFAs). similarly, honey contains two main monosaccharides (70% to 80%), glucose and fructose, and sucrose (<5%), and maple syrup consists mainly of glucose and fructose, which has a similar function to sucrose. Excessive intake may disrupt the structure of the gut microbiota, potentially promoting the growth of harmful bacteria (such as *Proteobacteria*) while reducing the abundance of beneficial bacteria (such as *Bacteroidetes*), which may lead to an inflammatory response[2]. This is due to the over-proliferation of certain bacteria that can utilize these sugars efficiently, and excessive levels of SCFAs can also have a detrimental effect on the gut, such as altering the pH, which consequently alters the balance of

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the gut microbiota.

#### 3.2.2 Indirect effects

While it is still unclear about if artificial sweeteners significantly impact both the composition and function of the gut microbiota, several possible mechanisms have been proposed regarding how artificial sweeteners indirectly influence gut microbiota.

Firstly, artificial sweeteners may affect gut microbiota by activating sweet taste receptors (e.g. T1R3) in the gut. Studies have shown that artificial sweeteners like aspartame, sucralose, and saccharin activate the sweet taste receptor T1R3 in the gut, which in turn affects the function of intestinal epithelial cells in terms of permeability and tight junctions[3]. Such activation may also contribute to the disruption of the intestinal barrier function and an increase in intestinal permeability, thereby affecting the composition and function of the gut microbiota.

Moreover, artificial sweeteners have been found to enhance the capacity of bacteria to form biofilms[4]. It enhanced the ability of model gut bacteria to adhere to, invade, and disrupt the host epithelium when co-cultured with human intestinal epithelial cells [5]. This implies that artificial sweeteners could influence gut health by modifying the composition and function of the gut microbiome.

## 4. Effects of Natural Sweeteners on Gut Microbiota

### 4.1 Sucrose, Honey, and Maple syrup

When exploring the influence of natural sweeteners on gut microbiota, particularly nutritive sweeteners, it is essential to consider how these sweeteners impact host metabolic health and their interactions with gut microorganisms.

Sucrose is widely used in the food industry and has been shown to be one of the major reasons for global obesity and metabolic disorders when consumed in excess[5].

In contrast, honey and maple syrup, contain various bioactive compounds, such as polyphenols and oligosaccharides, which may exert positive effects on the gut microbiota. For example, maple syrup has been found to reduce insulin resistance and lower hepatic fat accumulation, potentially due to its inhibition of gut α-glucosidase activity, a key process in carbohydrate digestion and absorption[5]. Additionally, an increased abundance of specific beneficial bacteria, such as *Faecalibaculum rodentium*, *Romboutsia ilealis*, and *Lactobacillus johnsonii*, has been observed with maple syrup consumption, which are involved in metabolism of carbohydrate, including utilizing sucrose and producing butyrate[5]. For honey, by inference, the oligosaccharides may serve as prebiotics, fostering the development of specific benefiting bacteria like *Bifidobacterium* species.

In summary, although sucrose, honey, and maple syrup are all nutritive, their impact on the gut microbiota differs. Sucrose may indirectly impact host health by altering gut microbiota composition, while honey and maple syrup may have more direct positive effects by providing nutrients or enhancing the development of specific beneficial bacterial populations. Future research would be required to further elucidate the specific mechanisms of these natural sweeteners and their long-term effects on human health.

### 4.2 Stevioside and Erythritol

In in vitro tests, steviol glycosides did not exhibit any impact on bacterial growth; however, erythritol was found to enhance the production of butyrate and valerate when tested with human gut microbiota[6]. Moreover, the application of steviol glycosides and erythritol in the Cebus apella model resulted in alterations in gut microbiota structural characteristics and diversity, though no adverse effects on the gut microbiome were observed[6]. This suggests that steviol glycosides and erythritol may affect host health by changing the composition and function of the gut microbiome.

Specifically, steviol glycosides are considered a safe, zero-calorie sugar substitute, with potential benefits for the host's gut microbiome, including an increase in microbial α-diversity[7]. However, another study indicated that 12 weeks of continuous steviol glycoside consumption did not alter the composition of the human gut microbiota[8]. This may imply that the impact of steviol glycosides on the gut microbiome is dependent on factors such as dosage, frequency of intake, and interactions with other dietary components[7].

Erythritol, a polyol found in nature, is also produced industrially through glucose fermentation. Erythritol is minimally fermented within the body, suggesting that it may not influence host health directly through modulation of gut microbiome function, as observed with other sweeteners.

## 5. Effects of Artificial Sweeteners on Gut Microbiota

While some studies suggest that artificial sweeteners may lead to dysbiosis (an increase in *Proteobacteria* and decrease in beneficial species such as *Akkermansia muciniphila*), potentially impacting host health[9], other research indicates that their effects on the gut microbiome are negligible[1]. This implies that the influence of artificial sweeteners on gut health may depend on various factors, including individual dietary habits, lifestyle, and the baseline composition of the gut microbiome.

Certain studies have indicated that long-term intake of specific artificial sweeteners may result in persistent changes to the gut microbiota, which could subsequently affect the host's health[11]. However, other research has reported that, even at high doses, artificial sweeteners have a limited impact on the gut microbiome in the short term[10]. The discrepancies in findings can be ascribed to variations in study design, such as the type of sweetener used, dosage, and the study population. Consequently, more high-quality clinical trials are required to accurately assess the specific impact of artificial sweetener consumption on the gut microbiome.

Recent studies found several specific species changed by artificial sweeteners. Multiple studies have demonstrated that NNS like aspartame, saccharin, and sucralose exhibit inhibitory effects on certain gut bacteria. For instance, saccharin and sucralose have been found to inhibit the growth of *Escherichia coli*[12]. Furthermore, sucralose has been shown to increase the proportion of *Firmicutes* in the context of a high-fat diet[12].

## 6. Health Implications of Altered Gut Microbiota Due to Sweeteners

Changes in the gut microbiome have been related to various health issues, including metabolic dysfunction, weight gain, and impaired glucose tolerance[4]. Notably, some studies have suggested that the intake of artificial sweeteners may lead to glucose intolerance and, in specific contexts, such as Crohn's disease models, the supplementation of artificial sweeteners can exacerbate gut inflammation and dysbiosis[13]. A study has found that artificially sweetened beverages (ASBs) intake is positively associated with the risk of type 2 diabetes in US adults[14]. In the study, 120 metabolites in participants' plasma were quantified by liquid chromatography-mass spectrometry and a metabolite profile associated with ASB intake was found related to a higher risk of type 2 diabetes[14].

Although most studies emphasize the unfavorable impact of artificial sweeteners on the gut microbiome, there is also evidence that certain types of sweeteners, such as stevia extracts, may have prebiotic functions, increasing the number of beneficial bacteria and enhancing the production of SCFAs. Certain sweeteners may help regulate gut inflammation and improve metabolic health by increasing the production of SCFAs[15]. The effects of sweeteners can also vary depending on specific disease models. For instance, in a mouse model of antibiotic-associated diarrhea, the addition of certain sweeteners, such as sorbitol, can alleviate symptoms, while others, such as sucrose, saccharin, and xylitol, may delay recovery[16].

## 7. Conclusion

This review examines the effects of both natural and artificial sweeteners on the gut microbiota. Natural sweeteners, such as honey and maple syrup, can promote the growth of beneficial bacteria, thereby enhancing the generation of short-chain fatty acids (SCFAs). In contrast, artificial sweeteners like aspartame and sucralose are associated with gut dysbiosis, potentially increasing the presence of harmful bacteria, such as *Proteobacteria phylum*. However, the impact of artificial sweeteners is inconsistent, varying based on the type of sweetener, dosage, and individual differences.

Existing studies are limited by focusing on short-term effects and often employ diverse research designs, which makes it challenging to draw consistent conclusions. The long-term effects of sweeteners on the gut microbiota remain largely unexplored. Therefore, future research should prioritize well-designed clinical trials to evaluate the long-term impacts of sweetener. Additionally, developing advanced methods to assess gut microbiota health and exploring personalized interventions are important directions for future research.

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